DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

RECOMBINANT DNA MOLECULE PROGRAM ADVISORY COMMITTEE

MINUTES OF MEETING

FEBRUARY 28, 1975

The Recombinant DNA Molecule Program Advisory Committee was convened for its first meeting at 9 a.m., February 28, 1975 in the Capri Room, Bellevue Hotel, San Francisco, California. Dr. DeWitt Stetten, Jr., Deputy Director for Science, presided for Dr. Ronald Lamont-Havers, Acting Director, National Institutes of Health. In accordance with Public Law 92-463 of January 5, 1973, the meeting was open to the public.

Committee members present were:

Dr. Edward A. Adelberg
Dr. Ernest H.Y. Chu
Dr. Roy Curtiss III
Dr. Stanley Falkow
Dr. Donald R. Helinski
Dr. David S. Hogness
Dr. Jane K. Setlow
Dr. Waclaw Szybalski
Dr. William J. Gartland, Acting Executive Secretary

A Committee roster is attached. (Attachment I)

Other National Institutes of Health staff attending were:

Dr. Leon Jacobs, Associate Director for Collaborative Research, OD
Dr. W. Emmett Barkley, Director, Office of Research Safety, NCI
Dr. Robert G. Martin, Laboratory of Molecular Biology, NIAMDD

National Science Foundation liaison representative was:

Dr. Herman W. Lewis, Head, Cellular Biology Section

Members of the Press present for portions of the meeting were:

Mr. Stuart Auerbach, Washington Post
Ms. Susan Ehmer, San Francisco Chronicle
Mr. Alan Kennedy, Medical World News
Ms. Gail McBride, JAMA Medical News
Mr. Frederic Moritz, Christian Science Monitor
Mr. David Perlman, San Francisco Chronicle
Ms. Judith Randal, Washington Star
Mr. Michael Rogers, Rolling Stone
Ms. Cristine Russell, BioScience
Ms. Janet Weinberg, Science News

I. CALL TO ORDER AND OPENING REMARKS

Dr. Stetten called the meeting to order and extended a welcome to the Committee members. With regard to situations requiring safeguards, he made reference to procedures devised for the handling of radioactive materials, and for the protection of human experimental subjects. Dr. Stetten said that the Committee would have to address itself to three general questions: 1) the conditions which the National Institutes of Health should impose on grantees and contractors working with recombinant DNA molecules, 2) the level of effort the National Institutes of Health should undertake to provide high containment facilities, and 3) the steps the National Institutes of Health should take to stimulate research which could reduce biohazards in this area.

Dr. Stetten assured the members that the National Institutes of Health had established the Committee as rapidly as feasible.

II. ROLE OF THE COMMITTEE

Dr. Jacobs told the Committee that the first meeting will be devoted mainly to procedural matters. He reviewed the functions with which the Committee is charged, namely: to provide advice concerning a program for the evaluation of potential biological and ecological hazards of DNA recombinants of various types, to develop procedures which will minimize the spread of hazardous molecules within human and other populations, and to devise guidelines to be followed by investigators working with potentially hazardous recombinants. Dr. Jacobs pointed out that the Committee has enough expertise to start work now on some of these problems. In addition, the Committee can call upon ad hoc consultants for advice, and can sponsor Workshops in given areas. Dr. Jacobs pointed out that the Committee was established in response to an appeal from the scientific community, and that there is no line item in the National Institutes of Health budget for the Committee or the programs it recommends.

There was discussion as to whether this Committee is to function as a national Committee. It was pointed out that the Committee is chartered to advise the Director, National Institutes of Health, but that it can interact with representatives of other agencies such as the National Science Foundation. For example, the National Science Foundation might choose to adopt the Committee recommendations.

With regard to membership, the Committee felt that representation of the areas of animal virology, plant pathology and epidemiology would be desirable. It was felt that the scope of the Committee should be broad at the beginning. The Committee specifically recommended that one lay representative be appointed. It was felt, however, that the Committee can not deal with ethical issues; it will have to restrict itself to considerations of safety and containment.

Although the name of the Committee will remain as is, it will limit itself to consideration of *in vitro* cell free experiments.

III. CONTAINMENT FACILITIES

There was discussion about the adequacy and convenience of present containment facilities. Dr. Barkley will prepare a list for the Committee of the approximately eighteen high containment facilities in the country. It was pointed out that most of these are not readily available to investigators outside of the facilities. The Committee felt that priority for establishment of high risk containment facilities is low at the present time. One national facility may be adequate at present. The Committee encouraged preservation of the Ft. Detrick facility for possible use for experiments requiring high containment. Dr. Barkley will communicate to the National Cancer Institute the Committee's evaluation of the necessity for containment facilities, and the possible utilization of Ft. Detrick.

With regard to the availability of moderate risk facilities, Dr. Jacobs said that the necessary equipment, such as laminar flow hoods, could be requested in grant and contract applications.

IV. INTERIM GUIDELINES AND IMPLEMENTATION

As an interim measure, and until further guidelines are elaborated, the Committee adopted, in general, the recommendations of the Asilomar Conference as stated in the "Provisional Statement of the Conference Proceedings."

The Committee recommended interim procedures for review of proposals involving work on recombinant DNA molecules. It was pointed out that the Asilomar Conference report is not yet a public document, and, therefore, can not be officially cited. However, other documents can be cited. It was suggested that for the time being, the National Institutes of Health send to applicants a copy of the Berg *et al.* letter and the Ashby report. Also as an interim policy, the applicant would file an appendix to the application providing information on: choice of vector, applicant's estimation of the potential biohazard, specifications of containment available, agreement to use sound microbiological procedures, statement of understanding of the Ashby report and the Asilomar Conference recommendations, etc. A suggested format for such an appendix is attached (Attachment II). The appendix would be reviewed by a local review group and then by the National Institutes of Health scientific review group.

The Committee felt that the concept of local review of applications is an integral and necessary part of the implementation of guidelines dealing with recombinant DNA molecules. It was the consensus of the Committee that institutional review committees should be established to certify procedures and facilities, but not to review applications for scientific merit. Local certification would be required for

applications proposing experiments in the moderate and high risk categories, but not for those in the low risk category. The certification statement would be attached to the application and would be required for acceptance of the application by the National Institutes of Health. The institutional committees would have the investigator's application, including the appendix, available to them, but would not pass on the scientific merit of the proposal. In other words, the institutional committee would judge the investigator's assessment of the risk, but not the quality and purpose of the research. If a given institution does not have the qualified staff for a local committee, a neighboring institution's committee, or perhaps a regional committee, could be utilized.

The National Institutes of Health Study Sections, in the course of scientific merit review, would judge the adequacy of the certification. The Study Section may disagree with the applicant that experiments are in the low risk category, and ask for certification by an institutional committee.

It was agreed that there will be no appeal of the institutional committees' decisions to the National Institutes of Health. However, the Recombinant DNA Molecule Program Advisory Committee will review appeals of Study Section judgments regarding adequacy of containment.

If during the course of the project period, the research changes direction significantly so as to increase the potential risk, the project would have to be evaluated again by the institutional committee and the National Institutes of Health. The National Institutes of Health should require reporting of such changes. It was felt that these procedures would induce investigators to conduct their experiments in a safer fashion if at all possible.

With regard to shipping of materials it was recommended that recombinants be defused by shipping as extracted DNA if possible. The DNA and the host should not be shipped in the same container.

V. STIMULATION OF RESEARCH

It was pointed out that the National Institutes of Health can use contracts to procure research in those areas in which protocols can be specified in advance. Grant applications can also be requested to stimulate research in specific areas. The latter would be assigned to the appropriate Institute for funding. Funding of these applications can not be guaranteed since there are no funds earmarked for the programs recommended by this Committee.

The properties of an ideal vector have already been enumerated. The Committee felt that the development of safer vectors is very urgent, and that much more work along these lines should be funded. It was felt that intense work on plasmids in particular should be encouraged. Care should be taken to avoid duplication of work in other countries. There needs to be a research program to test these new vectors to find out whether they

really are "safer." The testing will probably be carried out without additional funds.

The Committee agreed that epidemiological research needs to be stimulated. The members made a specific recommendation that an epidemiologist be appointed to the Committee.

The Committee recommended that the National Institutes of Health and the National Science Foundation advertise that they will entertain applications for the construction of safer vectors and in the area of epidemiology. An announcement will be placed in the National Institutes of Health Guide for Grants and Contracts, and an announcement will be requested in Science. Drs. Curtiss, Falkow, Helinski and Szybalski will work up draft National Institutes of Health announcements of interest for proposals in the areas of safer vectors and epidemiology. Dr. Falkow will collect information on plasmid ecology and what is known about their dissemination. This will help to decide if a contract program is necessary in this area.

The Committee agreed that a system to maximize the availability of strains and the communication of information is needed within the next few months. For example, a coordinating center for the vectors is needed. It was felt that any investigator, who constructs a safer vector, should inform the coordinating center.

Dr. Adelberg was asked to give serious consideration to expanding the E. coli K12 Genetic Stock Center at Yale to handle E. coli hosts. He said that the Stock Center would require some additional funds to handle the cells, but would be unable to handle the phage.

It was pointed out that many users of the stock materials will not be geneticists. Therefore, the supplier of the strains should be able to periodically check the strains.

A system for centrally distributing the information, such as a newsletter between constructors, testers and users of such vehicles is needed. Dr. Hogness will explore with Dr. Berg the responsibility for publication of such a newsletter. Dr. Helinski will keep in contact with Dr. Jacobs regarding possible National Institutes of Health publication of a newsletter.

Publications, such as Nature and Science, might be willing to run an announcement of the communication and distribution programs.

VI. WORKSHOPS IN SPECIFIC AREAS

The Committee felt that a scientific meeting to disseminate information on the construction of safer vectors would be desirable. It might be desirable to sponsor a workshop to consider experiments assessing the safety of strains and to decide what experiments need to be done. The Committee will consider the setting up of workshops in specific areas at its next meeting. It was also felt that training of workers in safe laboratory techniques is necessary.

VII. NEXT MEETING

At its next meeting the Committee will define a number of classes of containment and what falls within the various classes. The Executive Secretary will provide the members with background materials on safety and containment.

The next meeting of the Committee will be a two day meeting. The dates will be determined by the Executive Secretary. The Committee felt that Drs. Barkley and Martin should be present. Representatives of other interested agencies can also be invited.

VIII. ADJOURNMENT

The meeting of the Committee was adjourned at 5:00 p.m. on Friday, February 28, 1975.

I hereby certify that, to the best of my knowledge, the foregoing minutes and attachments are accurate and complete.

3/17/75
Date

DeWitt Stetten, Jr., M.D.
Acting Chairman, Recombinant DNA Molecule Program Advisory Committee
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William J. Gartland, Ph.D.
Acting Executive Secretary

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MARCH 1975

PROPOSED APPENDIX

My research involves (or does not involve) synthesis of recombinant DNA molecules between:

A. (specific details)

B.

My vector is the following:

I believe it is safe because:

I will follow rigorous and sound bacteriological procedures including sterilization of all biological materials before disposing of them.

I am aware of the following reports:

Any risk will comply with the specified principles in the following way:

1. Vector
2. Containment
3.